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Paul Ehrlich and Ludwig Darmstaedter Prize 2017 awarded to Pitt Cancer Researchers
Yuan Chang and Patrick Moore win prize for the discovery of two cancer viruses

Scientists looking for new tumor viruses have to keep an eye out for the virus genes rather than the viral particles. This year's winners of the Paul Ehrlich and Ludwig Darmstaedter Prize were twice successful with this strategy.

FRANKFURT am MAIN. Two Americans, Yuan Chang and Patrick S. Moore, will receive the 2017 Paul Ehrlich and Ludwig Darmstaedter Prize today in Frankfurt's Paulskirche for their discovery of the tumor viruses HHV-8 and MCV by means of a clever subtraction strategy. HHV-8 is the human herpesvirus 8, and MCV stands for Merkel cell polyomavirus. "With their decision to search for the viral genes rather than the viral particles, the prizewinners have taken a major step forward in the hunt for new human tumor viruses and have laid the foundation for further discoveries. The discovery of further human tumor viruses in future remains a distinct possibility," wrote the Scientific Council in substantiating its decision. One in every six cancers in the world is related to a viral infection. However, the risk of cancer from a viral infection is lower in the Western industrial countries than in the developing world. Yuan Chang is Professor of Pathology at the University of Pittsburgh Cancer Institute. Patrick Moore is Professor and Director of the Cancer Virology Program at the University of Pittsburgh Cancer Institute. They are a wife and husband team.

HHV-8 causes Kaposi's sarcoma, a tumor of the blood vessel cells, which can be seen on the skin with the naked eye owing to its pronounced red or purplish spots. The tumor occurs mainly in AIDS patients. In their search for HHV-8, Chang and Moore subtracted the entire human genome from the genomic DNA of the tumor cells. The idea behind this approach was that the remaining sequences would, in the best case, belong to the tumor virus and not to the human genome. Following this strategy, the prizewinners isolated two small DNA fragments

that they were eventually able to assign to a new herpesvirus. When they published their findings in 1994, they named the virus Kaposi's sarcoma-associated herpesvirus (KSHV). It was later given the official name HHV-8.

MCV is responsible for causing Merkel cell carcinoma, an extremely rare, malignant skin cancer. Chang and Moore refined their strategy in the search for the virus causing Merkel cell carcinoma. Fourteen years after the discovery of HHV-8, their approach was no longer to subtract the entire human genome from the tumor DNA but only the RNA sequences, thereby greatly simplifying the search. In addition, the sequences were not subtracted in a laboratory experiment but computationally, for which they used the published human genome sequences.

Chang and Moore not only discovered the viruses but also showed that they are in fact responsible for the two types of cancer. All Kaposi's sarcomas everywhere in the world contain HHV-8, in other words, not only those that occur in the context of AIDS but also the rare sarcomas that occur sporadically in the USA, Europe and Africa. The infection also precedes the tumor development. It was more difficult to demonstrate that MCV is the culprit in Merkel cell carcinoma because the virus is present in humans' normal skin flora. Chang and Moore showed that in all cells of a given Merkel cell carcinoma the virus is located at the same site in the genome – although the sites will differ between different Merkel cell carcinoma patients. The tumor must therefore have developed from a single cell with integrated MCV, and this fact, along with further findings, confirmed its causal role.

If some tumor viruses are ubiquitous, why does not everyone fall ill? The tumor viruses first have to overcome the cell's defenses – either by means of cancer genes that they bring with them as with HHV-8 or through mutations as with MCV – and the immune system has to be weakened for cancer to actually develop. Is there a vaccine or treatment for HHV-8 or MCV? "The situation with Kaposi's sarcoma is disappointing for us," says Moore. "Although the community of researchers has found candidates for a vaccine and target molecules for therapy, there is little commercial interest in developing a vaccine or a specific drug therapy." Chang adds: "For Merkel cell carcinoma, however, we're optimistic. Many patients respond to checkpoint inhibitors, some even go into complete remission." Checkpoint inhibition is a promising new therapeutic principle in cancer treatment.

The €120,000 Paul Ehrlich and Ludwig Darmstaedter Prize is among the most prestigious international awards granted in the Federal Republic of Germany in the field of medicine. The Prize will be presented by Professor Harald zur Hausen, Chairman of the Scientific Council.

Short biography of Prof. Yuan Chang

Yuan Chang (57 years of age) is a virologist and pathologist. She was born in Taiwan and grew up in Salt Lake City. She studied medicine at the University of Utah and holds a Bachelor of Science degree from Stanford University. Chang worked at Stanford University Medical Center, at the DNAX Research Institute of Molecular Biology in Palo Alto, and at Columbia University's College of Physicians and Surgeons in New York, before moving to the University of Pittsburgh in 2002. She is currently American Cancer Society Research Professor, Distinguished Professor of Pathology, and UPMC Endowed Chair in Cancer Virology at the University of Pittsburgh School of Medicine. Yuan Chang has won numerous

awards. This year she will receive the 2017 Passano Foundation Award together with her husband Patrick Moore.

Short biography of Prof. Patrick S. Moore

Patrick S. Moore (60 years of age) is an epidemiologist and virologist. He studied biology at Westminster College in Salt Lake City and completed his master's degree in chemistry at Stanford University. He studied medicine at the University of Utah and obtained a Master of Public Health at the University of California, Berkeley. He worked in Ghana in 1985 and then in Liberia in 1986. He then joined the Centers for Disease Control and Prevention, where he was involved in international public health interventions in Chad, Ethiopia, Saipan, Nigeria, Nepal and Somalia. He worked for a short time as Deputy Commissioner of the New York City Department of Health in 1993 before moving with his wife to Columbia University in New York. Moore was Professor of Public Health Division of Epidemiology at Columbia University until 2002, when he took up a position at the University of Pittsburgh. He is the Director of the Cancer Virology Program at the University of Pittsburgh Cancer Institute, American Cancer Society Research Professor, Distinguished Professor of Microbiology and Molecular Genetics and the Pittsburgh Foundation Chair in Innovative Cancer Research at the University of Pittsburgh School of Medicine. Patrick S. Moore has won numerous awards.

The Paul Ehrlich and Ludwig Darmstaedter Prize

The Paul Ehrlich and Ludwig Darmstaedter Prize is traditionally awarded on Paul Ehrlich's birthday, March 14, in the Paulskirche, Frankfurt. It honors scientists who have made significant contributions in Paul Ehrlich's field of research, in particular immunology, cancer research, microbiology, and chemotherapy. The Prize, which has been awarded since 1952, is financed by the German Federal Ministry of Health, the German association of research-based pharmaceutical company vfa e.V. and specially earmarked donations from companies. The prizewinner is selected by the Scientific Council of the Paul Ehrlich Foundation.

The Paul Ehrlich Foundation

The Paul Ehrlich Foundation is a legally dependent foundation which is managed in a fiduciary capacity by the Association of Friends and Sponsors of the Goethe University, Frankfurt. The Honorary Chairman of the Foundation, which was established by Hedwig Ehrlich in 1929, is the German Federal President, who also appoints the elected members of the Scientific Council and the Board of Trustees. The Chairman of the Scientific Council is Professor Harald zur Hausen, and the Chair of the Board of Trustees is Professor Dr. Jochen Maas, Head of Research and Development and Member of the Management Board, Sanofi-Aventis Deutschland GmbH. Professor Wilhelm Bender, in his function as Chair of the Association of Friends and Sponsors of the Goethe University, is Member of the Scientific Council. The President of the Goethe University is at the same time a member of the Board of Trustees.

Further information

You can obtain selected publications, the list of publications and a photograph of the laureates from the Press Office of the Paul Ehrlich Foundation, c/o Dr. Hildegard Kaulen, phone: +49 (0)6122/52718, email: h.k@kaulen.wi.shuttle.de and at www.paul-ehrlich-stiftung.de